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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CEPERLEY, MARY	

ART UNIT	PAPER NUMBER
1641	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,302	DIETRICH ET AL.	
	Examiner	Art Unit	
	Mary (Molly) E. Ceperley	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1 1/2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1) The third structure of Fig. 3 is missing the carbon atom of the terminal "-CO_2Me" moiety. A correction is required.

2) Although specific claims are cited in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

3) The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4) Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) It is unclear exactly what is being claimed in claim 1. Page 1, lines 3-10 of the specification describe "a proteinaceous compound...having a binding site for a group represented by the following formula (I)". Page 5, lines 12-17 further describes this "proteinaceous compound" as being "a compound which is capable of binding the above-described group of formula (I)". See also, the specification at page 7, lines 15-19 which indicates that the "proteinaceous compound according to the present invention" is "a polyclonal, monoclonal or recombinant antibody or functionally active derivative or fragment thereof". From these descriptions it is presumed that what is being claimed in claim 1 is an "antibody" specific for the compound of formula (I) rather than a "compound" which is comprised of "polypeptides". Clarification and appropriate amendment is required.

b) The claim 1 description of the "compound" as comprising "one or more polypeptides providing a binding site of a monoclonal,...antibody" renders the claim indefinite and confusing. What are the structures of the "one or more polypeptides"? Are these "one or more polypeptides", in fact, "antibodies"?

c) Claim 1 is indefinite in not defining the variable "R'".

d) In claim 1, it is unclear what structures are meant to be encompassed by the definition "R^1 and R^2 are connected to each other to form a cyclic moiety". Broadly interpreted, antibodies specific for compounds containing "a cyclic moiety" could include the well known microcystin-specific antibodies described in Nagata et al wherein the hapten contains a cyclic heptapeptide moiety (Natural Toxins 3: 78-86 (1995), Fig. 1). It is unclear how the given definitions of R^1 and R^2 could be combined to form "a cyclic moiety"; for example, it is unclear how R^1 defined as $-OSO_3$ could be combined with R^2 defined as "$(C_1$-$C_4)$carboxyaminoacyl" to form a ring structure or how R^1 defined as a halogen atom could be combined with R^2 defined as "$(C_1$-$C_4)$aminoacyl" to form a ring structure.

e) The claim 6 definitions of R^1 and R^2 are not encompassed by formula (I) of independent claim 1. See also, claim 19.

f) For claim 4, R^1 defined as "aminoacyl" is not a definition for R^1 as it is defined in independent claim 1.

g) The method steps of claim 9 will prepare an *immunogen* but not an *antibody* (i.e. the "compound according to claim 1"). See also, claims 21 and 22.

h) Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: steps which define a method of "use...for the detection of a compound". See also, claim 27.

i) The definition of R^1 in claim 19 as being "aminoacyl" is inconsistent with the definition of claim 1 wherein R^1 is "acylamino" (see the $-NR'_2$ definition of claim 2).

j) It is unclear what "compounds" (antibodies) are meant to be encompassed by claim 19. Are the different combinations of the recited variables meant to define a specific subset of compounds? How does the limitation "the toxin is selected from the group consisting of microcystin and nodularin congeners" relate to the remainder of the claim?

k) In claim 9, it is unclear what the complete structure is of the "compound *containing* a group represented by formula (I).

l) The claim 6 definitions of R^2 are not definitions which are encompassed by the R2 definitions of claim 1. See also, claim 19.

m) The claims are indefinite, confusing and incomplete in the use of the terms "a group represented by the following formula (I)" [claim 1] and "a compound containing a group represented by formula (I)" [claim 19] for the reason that the entire structure of the compound of which the "group" is one part is undefined/unspecified.

5) The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6) Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies prepared from a hapten of formula (I) wherein R^2 is "(C_1-C_4)acylamino" {i.e. R^2 is attached to the remainder of the molecule through a nitrogen atom as represented in the structures of Fig. 3}, does not reasonably provide enablement for antibodies prepared from a hapten of the formula (I) wherein R^2 is "(C_1 – C_4)aminoacyl". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

7) Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of immunogens using the haptens depicted in Fig. 3, does not reasonably provide enablement for the preparation of immunogens using the other structures encompassed by formula (I) of claim 1. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. For example, for the case in which R^1 is –O-alkyl or N-alkyl and R^2 is alkyl, there is no reactive functional moiety in formula (I) to which the immunogenic carrier could be attached to prepare the immunogen. Further, in claim 1, the terminal group $-C(O)R^1$ can be defined by terms such as $-C(O)OSO_3$ or $-C(O)OC(O)CH_3$ (R' = acyl as defined in claim 2) for which there is clearly no enablement in the specification.

8) Claims 11 and 21 are rejected under 35 USC 112, first paragraph, as not corresponding to the enabling written description of the invention as it is set forth in the specification. It is not clear that "plastic supports" and "polyethylene glycol" could be used as carriers to prepare the *immunogens* of claim 11. .

9) The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10) The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11) Claims 1-28 are rejected under 35 U.S.C. 103(a) as being obvious over ***a)*** Nagata et al (Natural Toxins 3: 78-86 (1995)) or An et al (Toxicon 32(12): 1495-1507 (1994)) taken alone or in combination with ***b)*** Humphrey et al (JACS 118: 11759-11770 (1996)).

The formula of instant claim 1 is the "Adda" moiety of *Microcystin* and *Nodularin* toxins. Nagata et al describe this "Adda" moiety of microcystins as being "the key functional domain of the microcystins" (page 84, first full paragraph). See also the statement in the Nagata et al reference regarding "the importance of the Adda structure for Mab binding" (page 82, the paragraph preceding TABLE III). An et al similarly describe the "Adda" moiety as being "essential for these toxins to express antibody specificity" (abstract of the article). See also, An et al at page 1503, first full paragraph, which states that "the configuration of the double bond in Adda is important for expressing the antibodies' specificity".

As set forth in the decision in *Ex parte Erlich* [3 USPQ2d 1011], given the teachings of the Nagata et al and An et al references that the "Adda" structure is a known epitope/antigen of microcystin, it would be obvious to prepare an antibody to the known "Adda" epitope/antigen, as claimed. This is particularly true given that Humphrey et al describes specific antigens encompassed by formula (I) of instant claim 1 (see Humphrey et al: page 11763, formulas **35** and **4**). The preparation of antibodies from known antigens and the use of these antibodies in immunoassays and affinity methods which utilize antigen-antibody binding (e.g. ELISAs) are well established in the art (see for example *Ex parte Erlich* [cited above], An et al: ELISA of page 1497; Nagata et al, Indirect Competitive ELISA of page 80). The packaging of reagents in kit form is an obvious expedient for ease and convenience in assay performance.

12) Claims 1-9 are rejected under 35 U.S.C. 102 (b)/103(a) as being unpatentable over each of Nagata et al (Natural Toxins 3: 78-86 (1995)) or An et al (Toxicon 32(12): 1495-1507 (1994)).

The antibodies of instant claims 1-9 have specificity for "a group represented by the following formula (I)". This "group" (an "Adda" moiety) is part of the *Microcystin* and *Nodularin* toxins as described in Nagata et al (Fig. 1) and An et al (Fig. 1). The antibodies of instant claims 1-9 are

considered to be functionally equivalent to and therefore anticipated by the antibodies of Nagata et al or An et al, i.e. both the claimed and reference antibodies are reactive with compounds which contain an "Adda" group.

13) Claims 10-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagata et al (Natural Toxins 3: 78-86 (1995)) or An et al (Toxicon 32(12): 1495-1507 (1994)).

The antibodies of claims 1-9 are anticipated by the references for the reasons set forth in paragraph ***12)*** above. The conventional preparation and methods of use of known antibodies and the packaging of antibodies in kits as set forth in instant claims 10-28 are well known in the art as described in paragraph ***11)*** above and are therefore rendered obvious by these prior art descriptions.

14) Metcalf et al (Wat. Res. 34(10): 2761-2769 (2000)) is cited to further show the state of the art.

15) Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (703) 308-4239. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556 or (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

August 30, 2003

Mary E. Ceperley

Mary (Molly) E. Ceperley
Primary Examiner
Art Unit 1641